UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/926,234	10/22/2001	Maria Marino	214038US0PCT	2544

22850 7590 07/12/2004

OBLON, SPIVAK, MCCLELLAND, MAIER & NEUSTADT, P.C.
1940 DUKE STREET
ALEXANDRIA, VA 22314

EXAMINER	
BUNNER, BRIDGET E	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 07/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/926,234	MARINO ET AL.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-7 and 10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-7 and 10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/24/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The finality of the Office action mailed is hereby withdrawn in view of the new ground of rejection set forth below.

Status of Application, Amendments and/or Claims

The amendment of 24 May 2004 has been entered in full. Claims 1-3, 8-9, and 11-13 are cancelled.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 4-7 and 10 are under consideration in the instant application.

Withdrawn Objections and/or Rejections

1. The objection to claims 1-3 and 8-13 at pg 3 of the previous Office Action (24 February 2004) is *withdrawn* in view of the cancelled claims (24 May 2004).

2. The rejection of claims 3, 8-9, and 13 under 35 U.S.C. § 112, first paragraph (enablement) as set forth at pg 3-8 of the previous Office Action (24 February 2004) are withdrawn in view of the cancelled claims (24 May 2004).

3. The supplemental information disclosure statement filed on 24 May 2004 has been considered.

Claim Rejections - 35 USC § 112, first paragraph

4. Claims 4-7 and 10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are directed to a peptide having the sequence of SEQ ID NO: 1 wherein R is H- or $COCH_3$, R' is COOH or $CONH_2$ and each amino acid has the L or D configuration. The claims recite a pharmaceutical composition comprising an effective does of a peptide compound having the sequence of SEQ ID NO: 1 wherein R is H- or $COCH_3$, R' is COOH or $CONH_2$ and each amino acid has the L or D configuration, and at least one pharmaceutically acceptable inert ingredient. The claims also recite a method of preventing the onset of Multiple Sclerosis in a human being, comprising administering to a patient an effective amount of a peptide compound having the sequence of SEQ ID NO: 1 wherein R is H- or $COCH_3$, R' is COOH or $CONH_2$ and each amino acid has the L or D configuration.

The specification teaches that the *in vivo* activity of the peptide of SEQ ID NO: 1 (formula 1) is evaluated on groups of SJL female mice, used at the age of 6-15 weeks. The specification also discloses that this strain of mice has been genetically selected for its ability to develop experimental allergic encephalitis (EAE) (pg 10, lines 26-30). The specification teaches that two groups of mice are immunized intraperitoneally with the peptide compound of formula I or II (pg 11, lines 1-5). The specification further discloses that after 2 weeks, EAE is induced all groups (including control) by challenge with P81-100 and mice are observed daily for clinical signs of EAE (pg 11, lines 8-22). Finally, the specification teaches that mice treated with the peptide of SEQ ID NO: 1 (formula 1) did not develop EAE (pg 12, lines 7-12; Table 1). However, the state of the art teaches that multiple sclerosis is a human autoimmune disease without fully effective treatment and largely unknown pathogenesis (including genetic factors) (Lutton et al., Exp Biol Med 229:12-20, 2004; pg 12, 1st paragraph; Pender et al., Intern Med J 32(11): 554-563, 2002; pg 555, col 1). The mouse model (EAE) is only an approach to study the

detailed pathological mechanisms, factors, and pathways that could provide specific targets for therapeutic strategies (t' Hart, Curr Opin Neurol 16 : 375-383, 2003, pg 377, 1st full ¶; pg 380, conclusion paragraph). t' Hart et al. also disclose that the cause of the neurological deficit in MS and EAE is still poorly understood and it is clear from animal models that CNS inflammation and demyelination do not fully account for the irreversible neurological deficit in advanced MS (pg 379. 1st full ¶). Therefore, a large quantity of experimentation would be required by the skilled artisan to prevent the onset of multiple sclerosis in humans. Also, t' Hart et al. indicate that an ideal animal model would reproduce all aspects of MS, such as susceptibility, clinical aspects, and histology (pg 377, 1st ¶; Table 1). Lutton et al. add that "more studies with a humanized animal model for MS may help clarify some of the differences between human MS and EAE in animals" (pg 17, concluding ¶). 't Hart et al. even indicate that there is a need for a valid preclinical model that is more closely related to the human disease (pg 379, last ¶ in col 1). t' Hart et al. teach that the common marmoset provides an excellent model that approximates chronic MS by the clinical and neuropathological presentation (pg 379, col 1-col 2).

Furthermore, Pender et al. state that "many therapies that are effective in the animal model, experimental encephalomyelitis (EAE), are either ineffective in MS or--in the case of gamma interferon, lenercept and alter peptide ligands--actually make MS worse" (pg 554, abstract). Therefore, undue experimentation would be required by the skilled artisan to prevent the onset of multiple sclerosis in humans by administering the peptide of SEQ ID NO: 1. Also, one skilled in the art would not be able to predict that prevention of EAE in mice with the peptide of SEQ ID NO: 1 would prevent multiple sclerosis in humans, as recited by the claims,

since human MS and EAE have differences and many therapies that were effective in EAE are ineffective in MS.

Additionally, since EAE is induced in mice by challenge with MBP fragment P81-100, isn't it possible that the claimed peptide of SEQ ID NO: 1 (compound I), which is a variant of P81-100, simply blocks the inducement of EAE since it is administered before the challenge? This mechanism would be a functional inactivation of T cells, rendering them incapable of eliciting an immune response to the P81-100 fragment. For example, relevant literature teaches that EAE in guinea pigs and rats can be suppressed if the animals are treated with MBP in IFA before or after immunization with MBP+CFA (Swanborg, R.H., Immunol Rev 184: 129-135, 2001; pg 131, 2nd full paragraph through the 4th full paragraph). However, as discussed above, since MS in humans is a complex auto-immune type disease with predominantly unknown etiology, one skilled in the art would not be able to predict that the peptide of SEQ ID NO: 1 prevents the onset of multiple sclerosis in a human being.

Due to the large quantity of experimentation necessary to prevent the onset of multiple sclerosis in humans by administration of the peptide of SEQ ID NO: 1, the lack of direction/guidance presented in the specification regarding the same, the complex nature of the invention, the state of the prior art indicating the differences in EAE and MS (see 't Hart et al., Lutton et al., Pender et al., and Swanborg), and the unpredictability of the effects of the claimed peptide in a human for the prevention of multiple sclerosis (see discussion and recited references), undue experimentation would be required of the skilled artisan to make and/or use the claimed invention.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (571) 272-0881. The examiner can normally be reached on 8:30-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

BEB
Art Unit 1647
07 July 2004

Brenda Brumback
BRENDA BRUMBACK
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600